ON THE VALUE OF THE ESTIMATION OF THE IONIC CALCIUM OF THE SERUM IN THE DIAGNOSIS OF, AND AS A GAUGE OF PROGRESS IN SPRUE

BY

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(*Received for publication* 15 *December*, 1924)

This contribution on the subject of sprue has a two-fold purpose. Firstly, to show the value of the estimation of the ' Ionic ' calcium as a diagnostic criterion ; secondly, to demonstrate that the same test, when repeated at intervals during the course of the disease, affords a valuable, in fact the most reliable gauge of progress.

Vines (1921) has shown that the calcium in the plasma normally exists in two forms. Of the total (10—11 mgm. per 100 c.c.) some 60 per cent. is readily precipitable by its chemical equivalent of ammonium oxalate solution, whereas the remaining 40 per cent., being ' bound,' probably with a lipoid complex, requires nearly three times its corresponding chemical equivalent. This latter, being closely concerned with the clotting of blood, is designated ' coagulative ' or ' combined ' calcium. When coagulation occurs, the latter becomes converted into the former, so that normal serum, as distinguished from plasma, contains all the calcium in the readily precipitable ' free ' or ' ionic ' form. If, on analysis of the serum, the total calcium is found to be normal in amount, whereas the ionic calcium is reduced, some of the calcium must have again become bound, and it is believed that the parathyroid glands, if acting normally, prevent this change.

An examination of this question, which is dealt with in Vines's work—*The Parathyroids in Relation to Disease* (1924), appears to show that ' there is no reason for assigning the control of calcium metabolism to any other endocrine gland ' nor can any other gland

' wholly or partially restore the disorders of calcium metabolism consequent on parathyroid failure or removal.'

It is clear that there may be two types of calcium deficiency, according as the total is decreased owing to there being an excessive excretion and a resultant calcium starvation of the tissues, or, the total being normal, the active or ionic calcium is deficient. In sprue the latter is the case. In very severe forms of the disease the total may be a little diminished, but never, as far as my observations go, to any marked extent. The error, therefore, would appear to be due, not to faulty absorption from the alimentary canal, but either to failure on the part of the tissues to use this calcium, or to errors in the regulation of calcium excretion—' a lowering of the threshold of excretion.' It is believed that in either case the underlying factor is a circulating toxin, which brings about the results found in sprue, by effecting a combination with the calcium of the blood or, perhaps, by damaging or interfering with the function of the parathyroids.

Further, toxaemias are said to stimulate thyroid function, and the antagonistic action of this gland to that of the parathyroid is well exemplified in sprue. If an impure preparation of parathyroid is used in treatment, that is, one containing any thyroid, or if, when progress is being made, parathyroid is stopped and thyroid given in its place, a return of the symptoms can be readily induced.

Dealing first with the value of the calcium estimation in diagnosis, it is particularly in diarrhoeic conditions that a reliable test is needed. We need not, therefore, discuss the diagnosis of diseases which are distinguishable on other clinical grounds. In pellagra, for example, there may be at times watery and offensive stools, with gastric and intestinal flatulence. There may also be a diffuse inflammation of the mouth. But these symptoms are clinically distinguishable from those in sprue, and there is nearly always a history of severe, bilaterally symmetrical ' sunburns ' in the spring, and evidence of pigmentation and roughness (pell' agra) on the back of the hands, the face and neck, to confirm the diagnosis.

In an article published recently in the *Journal of the American Medical Association* the writers Bastedo and Famulener (1923) discuss in full the means available for the diagnosis of sprue, cultural examination of bacteria, yeasts and so forth, and end by stating

'In sprue we have a disease for which no fully reliable laboratory criteria have been established.' I hope to demonstrate in the present paper that this no longer holds good.

In sprue it is the intestinal condition which first shows itself in the vast majority of cases—the early morning call to stool, with increasing bulk and frequency of pultaceous, frothy, fermenting motions. Intestinal disturbances are frequent in the tropics, and it is all-essential that treatment should be undertaken early. Accurate, and, if possible, early diagnosis is therefore most essential. The following is a brief account of a typical example :—

A man, aged 43 years, had spent most of the last twenty years abroad, having been in India, Africa, Mauritius, Ceylon, and the West Indies. For the past eight years he had suffered from loose actions of the bowels, the motions being yellowish or pale, sometimes frothy, and sometimes large. The condition had been diagnosed as malarial in nature, or more frequently merely as 'colitis,' and lastly as 'sprue.' He had submitted to various methods and courses of treatment with little if any benefit, and was finally sent to me definitely as a case of intractable sprue. The stool was certainly somewhat suggestive of that disease, fatty, greasy, unformed and bubbly.

The blood, however, showed a normal total and a normal ionic calcium content, and the faeces nothing particular except fat in excess. A second stool was found to contain *Entamoeba histolytica* cysts, and the probabilities were that the whole trouble was a residual dysenteric condition, the fat being due to the milk diet to which he had been restricted for a long period. Injections of emetine and a course of emetine bismuthous iodide cleared things up. There was no sprue.

Cases like this are comparatively common and I have, therefore, for some months past been examining the blood from patients at the Tropical Diseases Hospital and elsewhere in order to see whether this peculiar condition of the calcium—reduction of the ionic with a normal or nearly normal total—occurred in other diseases in which there was diarrhoea as a prominent symptom especially diarrhoea of a sprue-like nature. The method employed has been that devised by Dr. H. W. C. Vines (1921).

The following Tables will save pages of description :

TABLE I

Showing the Calcium content of the serum of Sprue patients before treatment

Initials	Ionic Ca.	Total Ca.	Initials	Ionic Ca.	Total Ca.
	%	%		%	%
Fr.	7·7	10·1	Ly.	6·9	9·9
Td.	6·8	9·9	J.T.	7·9	10·0
C.	6·9	9·8	R.*	8·1	10·4
L.E.B. ...	6·3	10·1	B.	6·9	9·9
A.W.	7·3	10·4	Bp.	6·6	9·9
E.	7·3	9·9	Bi.	7·9	10·0
Ge.	7·1	10·8	Ln.	6·3	9·9
R.W.	6·3	9·9	Tr.	7·7	10·1
St.	6·6	9·8	Ws.	7·1	10·1
R.P.W. ...	6·9	9·8	Es.	7·9	9·9
McG.	6·1	9·9	H.S.	7·0	9·9
Cr.	7·9	10·1	McC.	6·6	10·0
Ln.	6·6	9·8	Ts.	7·7	10·5
Ct.	6·6	10·1	Hn.	6·6	10·2
Bn.	6 1	10·6	Ee.	6·4	10·4
Rl.	6·7	10·4	Cm.†	6·1	9·4

* A mild case ; had been under treatment outside

† Very ill ; died within twenty-four hours

TABLE II

Showing the Ionic Calcium of the serum of patients other than Sprue

Disease	Initials	Ionic Ca.	Disease	Initials	Ionic Ca.
		%			%
Dysentery Amoebic ...	Ke.	10·6	Dysentery Bacillary ...	P.L.W. ...	11·5
,, ...	Ma.	10·6	,, ...	Ka.	10·6
,, ...	Me.	10·4	,, ...	M.T. ...	10·6
,, ...	Cr.	10·0	,, ...	Wa.	9·9
,, ...	D.S.	10·4	,, ...	S.R. ...	10·4
,, ...	B.S.	10·6	,, ...	W.S. ...	10·4
,, ...	H.E.	10·4	,, ...	M.D. ...	10·6
,, ...	Sn.	9·9	,, ...	T.R.	10·6
,, ...	J.N.R.A. ...	11·0	,, ...	So.	10·6
,, ...	S.N.	9·5	,, ...	B.N.	10·4
,, ...	Co.	10·6	,, ...	Sm.	10·6
,, ...	C.N. ...	10·4	,, ...	Jn.	10·1
,, ...	W.N. ...	10·1	Mucous colitis	O'B	10·4
,, ...	P.T.	10·6	,, ...	N.N. ...	10·4
,, ...	J.N. ...	10·6	,, ...	B.	10·6
,, ...	K.F.	10·4	,, ...	G.R. ...	10·1
,, ...	Mi.	10·7	,, ...	F.N. ...	10·1
,, ...	T.R.	10·0	,, ...	Bi.	11·1
,, ...	Bk.	10·4	Ulcerative colitis ...	Br.	10·6
,, ...	Cr.	10·6	Syphilis ...	A.W. ...	10·6
,, ...	Jn.	10·0	,, ...	W.	10·6
,, ...	Pe.	10·4	,, ...	N.	10·6
,, ...	Ds.	11·1	,, ...	R.	10·1
,, ...	Pt.	10·4	,, ...	Wr.	10·4
,, ...	Sy.	10·2	,, ...	B.	10·6
,, ...	E.	10·4	,, ...	C.H. ...	10·6

TABLE II—*continued*

Disease	Initials	Ionic Ca.	Disease	Initials	Ionic Ca.
		%			%
Syphilis ...	Na.	10·4	Malaria (M.T.)	El.	9·8
,, ...	A.	10·6	,, ,, ...	Ko.	10·2
Malaria (B.T.)	C.	10·4	,, ,, ...	Bo.	10·4
,, ,, ...	C.E.... ...	10·6	,, ,, ...	To.	9·4
,, ,, ...	H.*	9·5	,, ,, ...	La.	10·6
,, ,, ...	D.	9·9	,, ,, ...	H.B.... ...	9·6
,, ,, ...	B.	9·1	,, ,, ...	Dn.	10·2
,, ,, ...	M.	10·1	,, ,, ...	Mn. ...	9·4
,, ,, ...	Eg.	10·4			
,, ,, ...	Bl.	10·4	Kala azar ...	Mo.... ...	10·4
,, ,, ...	Om. ...	10·4			
,, ,, ...	Cr.	9·9	Trypanosomiasis	W.	10·1
,, ,, ...	Ch.	10·6	General Paralysis (treated by malaria)	Ma.	9·9
,, (M.T.)	Wa.* ...	9·1			
,, ,, ...	B.R.... ...	9·9			
,, ,, ...	W.	9·8	Filariasis ...	W.	10·1
,, ,, ...	B.O.... ...	9·9	,, (?) ...	B.	10·6
,, ,, ...	S.	10·4			
,, ,, ...	C.	9·5	Beriberi ...	C.	9·9
,, ,, ...	A.	10·1	,, ...	F.C.... ...	10·4
,, ,, ...	Pr.	9·2	,, ...	C.L.... ...	10·4
,, ,, ...	Cl.	9·1	Jaundice and diarrhoea	D.	10·6
,, ,, ...	Ch.	8·9	,, ...	S.	10·2
,, ,, ...	Hd.	9·7	Undulant fever	B.	10·7
,, ,, ...	F.C.... ...	9·7	Tuberculosis ...	P.	10·4
,, ,, ...	K.	9·7	Endocarditis ...	R.	10·4
,, ,, ...	R.	9·1	Tapeworm ...	S.	10·6
,, ,, ...	L.	10·1	Ankylostomiasis	L.	10·2
,, ,, ...	T.	9·1	Ascariasis, &c....	F.	10·6

* These had Syphilis also

B.T. = *Pl. vivax* infection.

M.T. = *Pl. falciparum* infection.

Table I is a list of cases of sprue whose blood was examined on their first coming to hospital or within a week or so, that is, before sufficient time had elapsed for any treatment to have had an appreciable effect on the calcium content.

From this it will be seen that the total calcium is but very little reduced, whereas the ionic calcium is between 20 and 30 per cent. below the normal.

Table II gives the amount of ionic calcium, as before in mgms. per 100 c.c. in the serum of patients other than sprue, many of them with diarrhoeic symptoms. Others have also been included as a matter of interest. It will be seen that those conditions most likely to be confounded with sprue, namely, the dysenteries and forms of colitis, are all about the normal limit as regards the ionic calcium. It is worthy of note also that the only common tropical affection in which there is a fairly consistent reduction is that of malaria, and in the one case of general paralysis of the insane which was being treated by malaria.* But in none of the malarial patients whose blood was examined was the reduction of the ionic calcium anything like so great as that found in sprue. This, moreover, is not of much importance in practice, for it would only be in those not very common cases in which diarrhoea was associated with malaria as a prominent symptom that the question of diagnosis would arise at all.

It is clear, therefore, that the estimation of the ionic calcium is a very useful factor in diagnosis of sprue from other diarrhoeal conditions, and, since accurate diagnosis forms the basis of rational treatment, a test which will establish the diagnosis of an obscure disease such as is sprue from others with sprue-like symptoms becomes of considerable medical importance.

Passing to the second part of this paper—the value of the estimation of the ionic calcium of the serum in gauging the progress of disease in Sprue.

Important as the test is in diagnosis, it is vastly more important and more useful as an indication of progress. If all is going well and the serum is examined at intervals of a fortnight, or, better still, a week, the percentage of ionic calcium is found to rise steadily to

* This is of interest seeing that cases of chronic malaria have been recorded of late in which marked improvement followed the administration of parathyroid.

the normal. Any return of symptoms, such, for example, as a sore or tender tongue, or the reappearance of a few aphthae in the mouth, is accompanied by a drop in the ionic, not the total, calcium. Such may arise from an attempt to increase diet too rapidly or unduly hurry the convalescence, and may be, usually is, a warning of a relapse, and, if regarded as a mere ' upset from indigestion ' and the warning allowed to pass unheeded, a relapse will certainly take place, necessitating the loss of several days, perhaps weeks, in the cure. If, however, the calcium content is determined and is found to have dropped, a return to milk for a couple of days or so will usually suffice to restore the balance and progress will then continue. If, on the other hand, it is found to have maintained its level, the symptom is of no practical importance and the fuller diet need not be curtailed.

To avoid repetition this aspect of the question may be dealt with briefly under the following headings :—

1. Ionic calcium is always low in the untreated disease, even in the early stages.
2. The ionic calcium increases as the condition improves.
3. The ionic calcium falls again if a relapse occurs.
4. Improvement takes place when calcium is administered alone, but is slower and less stable than when parathyroid is given in addition.
5. Improvement, evidenced by the clinical condition and, more accurately, by the rise in the ionic calcium, is more steady and more rapid when parathyroid is given.

1. This first point need not be further elaborated. It is abundantly proved by what has gone before in showing the value of the test in diagnosis, and the table (Table I) affords many examples.

2. The ionic calcium increases as the patient's condition improves. The following is an illustrative case.

J.T., aged 35 years, had suffered from sprue for eight months. His condition had been diagnosed, first as amoebic dysentery and, later, as colitis, but treatment for these had been unavailing. The symptoms were typical—sore mouth and tongue, with ulceration, flatulence, acidity, large, pale, frothy stools, cramps and loss of weight. At commencement of treatment the ionic calcium was low, 6·8 mgm. per cent. ; three weeks later there was no longer any soreness of the mouth, the stools were less frothy and bulky, and the dyspepsia was less. The ionic calcium was now 7·9 per cent. ; the total had remained about normal, 10·4 per cent. A fortnight later there was great general improvement ; the patient felt

stronger, no longer suffered from lassitude or depression, had only one action of the bowels daily, and that was normal, was on a fairly generous diet and was getting up for three or four hours each day. The ionic calcium was now 8·8 per cent.; in yet another fortnight he 'felt well,' and the calcium was 9·5 per cent., and a week later 10·4, the same as the total calcium. He left the nursing home, taking full diet, and went to Scotland, where he played golf and, in fact, lived a normal life, and ceased to take any medicine. Two months later he wrote to say that he was keeping 'quite fit,' and four months afterwards he was in London and called to show himself. He looked the picture of health, and opportunity was taken to test his blood again. It had more than maintained the previous level, being now at the upper limit of the normal, namely 11·1 per cent. This patient has returned to the tropics.

3. The ionic calcium falls again below the former level if a relapse occurs.

F.W.W., 31 years; duration of typical sprue symptoms six months. When the blood was first examined, after three weeks' treatment, the ionic calcium was 8·1 and the total 10·6 per cent. He made excellent progress and the ionic calcium was found to be 10·6 per cent. three and a half weeks later. He was then allowed full diet and to do more or less as he liked, getting up and going about. In fact, he tried to go along too quickly. In two weeks the mouth began to feel sore, and the stools were a little more bulky and pale. He was, in short, starting to relapse. Another examination of his blood was made and it was found that though the total calcium had remained at 10·6, the ionic had fallen again to 8·5 per cent. The diet had to be reduced and treatment begun again. In another month he was well and able to go out, and there has been no report of any recurrence of symptoms.

This point is important enough to warrant the recording of a second case, which was more severe than the last.

A.C., female, 51 years, had suffered for two years or more from sprue, with frequent relapses. All the typical symptoms were present, the mouth symptoms—soreness, tenderness and ulceration of tongue and buccal mucous membrane—being very pronounced. The ionic calcium before she started treatment was as low as 6·9 mgm. per cent.; three weeks later all the symptoms were much improved. She felt stronger and was getting up for an hour or two daily, and the ionic calcium had increased to 8·1 per cent. In another fortnight it had reached normal, 10·6, and a fortnight later still had increased to what is regarded as the upper limit of the normal, 11·6 per cent. Four weeks later the tongue began to feel tender, two small aphthae appeared, and she began to pass paler motions. The blood was sent up and it was found that the ionic calcium had fallen again to the lower limit of the normal, 10·2 per cent. A return to milk for three days, with a resumption of the medicine, cleared up these symptoms, which, if disregarded, would, as on former occasions, most certainly have been the forerunners of a severe relapse.

4. The mode of treatment has a distinct effect upon the rate of progress, and this is best gauged by the ionic calcium estimation. The disease having been shown to be associated with a deficiency in this substance, treatment by calcium in some form leads to improvement of symptoms, though, if given alone (that is, without

parathyroid) this improvement is slow and not very stable. As an example of the former the following may be very briefly narrated :—

G., male ; a fairly severe case treated on the ordinary lines—diet (chiefly milk) and rest in bed, but without parathyroid. After ten weeks, the ionic calcium was only 7·1 per cent., though improvement had been steady but very gradual. Three weeks later it had risen to 8·3 per cent. only, and in another three weeks (i.e., after sixteen weeks' treatment) it was still below normal, namely 9·1 per cent., though the total was 10·6. Clinically speaking, he was nearly well, was up and about, but on a limited diet still, and shortly afterwards he left hospital. Unless he is very careful he is almost certain to relapse, and that probably before very long.

The following is an illustrative example of the instability of treatment by calcium alone.

H.B., 40 years. After twelve weeks in hospital this patient was up and about, though on a restricted diet, and was to all appearances well, and was on the point of leaving. Without any reason being discovered, and while he was on the restricted diet and under a cautious régime, he again lost weight and expressed himself as ' not feeling quite so well.' His blood was taken and the ionic calcium was found to have fallen to 9·5 per cent., though the total was normal, 10·6 per cent. The diet was therefore again reduced, and he was made to return to bed ; in three weeks the ionic calcium was again normal, 10·4, but he was not considered well enough to leave hospital for another two months.

These two cases are good instances for showing that it is not absorption of calcium which is defective, but the proper regulation of it after it has been absorbed.

5. Lastly, the improvement, as evidenced both by the clinical condition and by the rise in the ionic calcium of the serum, is more rapid when, in addition to the administration of the calcium, parathyroid is also given to regulate its metabolism. Previous papers (see References) afford many examples of this, but to render the present paper more complete the following may be briefly narrated.

(1) A. McG., male, 28 years of age. Ill for ten months with the typical symptoms of sprue. He had lost 28 lbs., in weight, had a sore and tender tongue and mouth, and was passing frothy, pale and rather bulky stools. When admitted to hospital his ionic calcium was down to 6·1 mgm. per cent. He was given calcium in the form of milk and also cachets of the lactate, gr. 15, thrice daily, and parathyroid, gr. 1/10 of the dried extract, twice a day. He reacted wonderfully well. In a week the ionic calcium was 8·1, and in a fortnight 10·1 per cent., the total being close upon normal, 9·9 per cent. on the first two occasions, and 10·1 on the third. He remained in hospital for another five and a half weeks, steadily maintaining his improvement, and left after a stay of less than eight weeks. The ionic calcium when he went out was 10·8 per cent.

(2) S., male, 48 years. This was a more severe case and one of longer standing, having existed for over two and a half years. When admitted to hospital he was 36 lbs. below his normal weight. He was at once given the same treatment as the patient whose case has just been described—calcium lactate gr. 15, three times, and extract parathyroid gr. 1/10, twice daily. The symptoms steadily and rapidly improved and he left hospital thirty-one days after admission, feeling and looking very well.

After one week's treatment the ionic calcium was 7·0 per cent.; after two weeks 7·4; after three weeks 10·8, and it had remained there when he left. More than six months later he came to show himself. He had taken no medicine during that period and had kept perfectly well, and had not had to restrict his diet or smoking in any way. He was a heavy smoker and the soreness of the mouth, by depriving him of this solace, caused him great distress. His blood was taken to see if the calcium content had been maintained, and it was found that his own parathyroids were carrying on their work satisfactorily, and that absorption of calcium was very good. The ionic and the total were the same, 11·1 per cent.

(3) A.B.W., female, 34 years. This case, though not of so long duration, only twelve months, was exceptionally severe. At times she had as many as fifteen copious, loose, frothy, pale stools in the twenty-four hours; her tongue was very sore and ulcerated; she had troublesome cramps, and had lost 42 lbs. in two months. She then started calcium lactate and parathyroid, but both of them in too small doses; of the former gr. 5 thrice daily, of the latter gr. 1/20 twice. When seen two months later, on her arrival from abroad, the tongue and mouth were very sore, red, and tender, and she was obviously ill. The stools, however, had been reduced to four daily. The ionic calcium was at this time 7·3 per cent. She was at once put on an increased dose of calcium, namely gr. 15 of the lactate three times a day, and the dose of the parathyroid was doubled. The change was remarkable; within fourteen days the number of stools was reduced to one daily, no longer frothy, and much less bulky. In another week she had to take liquid paraffin to overcome constipation, and was progressing so well that she was able to sit up for some hours each day. The serum calcium (ionic) had increased to 9·5 per cent.; in another fortnight she was going for walks, was taking a diet comprising milk and milk puddings, bread and butter, eggs, fish, chicken and fruit. The stools were normal in size and colour, and only one in the twenty-four hours. The ionic calcium was now 10·1 per cent. Two weeks later, that is seven weeks after I first saw her, she came to London from Bristol, looking well, and taking all food without discomfort. Another blood examination showed a normal calcium content, 10·6 per cent. It was considered that the food now contained abundant calcium, and, since absorption had not been upset, the total having been practically normal throughout, this element was omitted from the medicine. The dose of parathyroid was reduced in order to test whether her own glands were now capable of carrying on their function and instructions were given that, if no untoward symptoms arose, it, in turn, was to be stopped altogether after another week. This programme was carried out and three weeks later she again travelled up from Bristol, this time to visit the Wembley Exhibition. She had had no treatment of any kind during the previous fortnight, but the calcium content of the blood was fully maintained, being now 11·1 per cent.

I saw her finally four weeks afterwards; she looked the picture of health, stated that she felt better than she had done for years and full of energy, that she was going about all day, eating anything put before her; in fact, living a normal life, and was arranging to return to India.

A last examination of the blood was made and gave ionic calcium 11·1 per cent., no residual, coagulative, combined calcium. This patient wrote five months later to say that she was in perfect health, eating heartily without any restrictions, had more than maintained her weight, was doing hard work (as a missionary) and 'felt full of energy.'

These facts are demonstrated in the accompanying Tables III and IV.

TABLE III

Sprue Cases under Ordinary Treatment
Showing the Gradual Rise in the Ionic Calcium

Ionic Calcium in mgms. per 100 c.c. serum.

Initials	Before treatment	Number of weeks after starting treatment											
		1	2	3	4	6	8	10	12	14	16	18	20
F. ...	...	7·7	...	...	9·1	...	...	...	...	...	...	...	...
L. ...	...	...	...	6·9	...	...	9·1	...	...	10·1	...	...	...
Ln. ...	6·6	...	...	...	...	9·9	...	...	...	...	...	...	...
H.W.B.	...	...	...	...	...	...	...	...	9·3	...	10·4	...	...
G. ...	...	...	...	...	...	...	7·1	...	...	8·3	...	...	9·1
L.O. ...	...	6·3	...	...	...	...	...	9·9	...	...	...	...	...

TABLE IV

Sprue Cases Treated by Parathyroid in Addition
Showing the more rapid Return of the Ionic Calcium to Normal

Ionic Calcium in mgms. per 100 c.c. serum

Initials	Before treatment	Number of weeks after starting treatment								Remarks
		1	2	3	4	6	8	10	12	
J.T. ...	...	7·9	...	8·8	...	9·5	10·4	...	11·1	Still 11·1 when seen 4 months after ceasing to take any medicine.
M.C....	6·9	...	8·1	...	10·5	...	11·6	...	...	
A.W. ...	...	7·3	...	9·5	...	10·1	10·6	...	11·1	Maintained when seen 2 months after. Reported as 'perfectly well' 7 months after.
H.E. ...	...	7·3	...	...	...	...	...	10·6	...	
E.J.W.	...	...	8·0	...	8·9	10·4	...	10·8	...	11·0 when seen 3 months after ceasing medicine.
McG.	6·1	8·1	10·1	...	...	10·8	...	...	...	
H.S. ...	...	7·0	7·4	10·8	10·8	...	...	...	...	11·1 when seen 6½ months later.
W.E. ...	6·9	7·4	8·7	9·7	10·4	...	...	...	...	Living a busy, active life and 'feeling full of energy' 6 months later.
S. ...	6·6	...	7·7	...	9·7	10·4	...	...	...	Gone abroad; keeping well.
E. ...	...	...	7·1	...	10·3	...	11·1	...	...	

I desire to express my thanks to those who either sent or allowed me to take specimens of blood for these tests, especially Professor T. R. Elliott, F.R.S., Director of the Medical Unit, University College Hospital; Dr. G. C. Low and Dr. P. H. Manson-Bahr, Physicians to the Tropical Diseases Hospital; Dr. H. B. Newham, Pathologist to the Tropical Diseases Hospital; Colonel C. Barry, I.M.S. (ret.), and Dr. H. S. Stannus.

SUMMARY

1. Sprue is a disease which is constantly associated with a fall in the amount of ionic calcium in the serum, whereas the total remains at or about normal.

2. A rise and fall of the ionic calcium coincides with improvement and relapse.

3. Absorption of calcium is little, if at all, interfered with, but calcium metabolism is upset.

4. Consideration of this fact and of some of the other symptoms of sprue, especially the cramps and tetany in severe or advanced cases, points to interference with the function of the parathyroid glands.

5. Amelioration of symptoms, followed by cure, is obtained by oral administration of suitable salts of calcium and a pure and active preparation of parathyroid in adequate doses.

6. The period needed for cure by these means is much shorter than by previous methods, the main symptoms clearing up in some cases within a few days. The administration of the parathyroid must, however, be maintained to stabilise the amelioration, but no ill-effects have been found to occur if it be continued longer than is actually necessary to bring about this result.

7. In the light of the above it is interesting to note that most of the old, empiric remedies contain lime as an important constituent.

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